Metabolic Physiology in Pregnancy

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Abstract

The metabolic physiology during pregnancy is unique in the life of women. This change is a normal physiological adaptation to better accommodate the foetal growth and provides adequate blood, nutrition and oxygen. The metabolic changes prepare the mother's body for pregnancy, childbirth and lactation. Early gestational period is considered as an anabolic phase, in which female body stores nutrients, enhance insulin sensitivity to encounter the maternal and feto-placental demands of late gestation and lactation. However, late gestational period is better named as a catabolic phase with reduced insulin sensitivity. The placenta plays a role as a sensor between mother and foetus physiology and acclimatizes the needs of the foetus to adequate growth and development. During pregnancy the female body changes its physiological and homeostatic mechanisms to meet the physiological needs of the foetus. However, if the maternal metabolic physiology during pregnancy is disturbed, it can cause hormonal imbalance, fat accumulation, decreased insulin sensitivity, increased insulin resistance and even gestational diabetes mellitus.

Keywords: Pregnancy, Metabolic changes, Physiological changes.

Introduction

The metabolic process is the biochemical mechanism occurring within a living cell and is necessary for the maintenance of life process. Pregnancy (gravidity or gestation) is the time period from day of conception to the delivery during which embryo and later on the foetus develops inside a female uterus. Pregnancy causes multiple, regular, anatomical, physiologic adjustments that affect the body metabolism. The physiological adjustments vary from female to female depending on her environment, physical status, lifestyle behaviour, pre-pregnancy nutrition, maternal and foetal genetic constitutions. Maternal physiology during pregnancy is categorized by hormonal and metabolic modification in order to maintain constant foetal requirements for nutrition, blood and oxygen. As pregnancy progresses a great adaptation in the maternal endocrine metabolism occurs mainly through the hypothalamus and its connection with various endocrine glands.

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Hypothalamic Endocrine System

The hypothalamic endocrine system is a key control center for most of the maternal endocrine system. The Hypothalamus consists of multiple small nuclei with variety of functions. Hypothalamus is anatomically and physiologically linked to Central Nervous System (CNS) and endocrine system through paracrine and autocrine signaling. The maternal hormonal adaptations encompass sensing with endocrine system including anterior and posterior pituitary gland, thyroid and parathyroid glands, adrenal glands, ovary and uterus which interact with foetal-placental-maternal interface.

Maternal hypothalamic-pituitary-adrenal axis system (HPA)

In pregnancy, maternal "hypothalamic-pituitary-adrenal (HPA) axis" experiences continuing modification due to assembly of "Corticotrophin-Releasing Hormone" (CRH).[1] CRH is synthesized by para-ventricular nucleus of the hypothalamus and enhances the release of "Adreno-Corticotrophin Hormone" (ACTH) by anterior pituitary gland. In turn, "ACTH" stimulates the adrenal cortex to secrete cortisol into bloodstream.[2] Increase placental synthesis of estrogen enhances the hepatic "corticosteroid-binding globulin" (CBG), thus increasing free and bound cortisol. Plasma ACTH concentration cause a parallel rise in the cortisol.[3] In pregnancy, the hypothalamic stimulatory hormones including "growth hormone-releasing hormone GHRH", "gonadotropin-releasing hormone GnRH", "corticotropin-releasing hormone CRH" and "thyrotropin-releasing hormone TRH" are increased4. The suppressing hypothalamic hormones such as "prolactin-inhibiting factor" and "somatostatin" also augment to make a physiological symmetry between the endocrine arrangements and pregnancy demand.[4]

Pregnancy and Pituitary

The normal female pregnancy has melodramatic impact on the "maternal hypothalamic-pituitary-adrenal axis system".[2,3] Pregnancy increases the "17-hydroxysteroids 17-hydroxycorticosteroids (17-OHCS)", "total and free plasma cortisol", "urine free cortisol (UFC)" and CBG values.[5] The free cortisol concentrations decreases transiently as CBG increases. However, free cortisol

increases particularly during the 2nd and 3rd trimesters. As pregnancy progresses hypo-thalamic and pituitary hormone secretion is decreased, although, circulating levels increase due to placental production of biochemically identical hormones.[6] Amongst anterior pituitary gland hormones, "growth hormone" (GH) synthesis decreases, however, "placental-like growth hormone" increases in the third trimester of the pregnancy. There is also an increase in "adrenocorticotropic hormone (ACTH)" and "thyrotropin (TSH)" hormone. The intermediate lobe of the pituitary gland secretes "melanocyte-stimulating hormone" (MSH) that causes skin hyper-pigmentation during pregnancy.

The supra-optic nuclei of the hypothalamus synthesize "antidiuretic hormone" (ADH) and paraventricular nuclei of the hypothalamus secrete "oxytocin". Both hormones are stored in the posterior pituitary gland. The gradual upsurge in maternal plasma fluid is due to the pregnancy-allied hormones that decrease marginal vascular resistance to activate the "renin-angiotensin-aldosterone system", Pregnancy amplifies the ADH discharge, fluid retention to maintain blood pressure.[7]

Pregnancy and Thyroid Hormones

In thyroid physiology, pregnancy brings about many physiological changes including increased plasma volume and renal clearance.[8] In pregnancy, the basal metabolic rate (BMR) is increased that results in tachycardia. To encounter the increased metabolic requirements during pregnancy, two folds increase is observed in serum "thyroxine-binding globulin" (TBG) and "thyrotropin" (TSH) receptor stimulation by human "chorionic gonadotropin" (HCG). To retain the ample free "thyroid hormone" levels during the pregnancy, "thyroxine (T4)" and "triiodothyronine (T3)" synthesis increase in the first half of pregnancy and the overall synthesis rate of thyroid hormones returns to pre-pregnancy conditions.[9]

Pregnancy and Adrenal Gland Response (Catecholamines)

The first trimester of pregnancy is allied with considerable, dynamic adaptations in cardio-vascular autonomic nervous system (ANS) with increase in sympathetic and decreases in parasympathetic activity[10] that results an upsurge in heart, respiratory rate, stroke volume and cardiac output. Sympathetic stimulation during pregnancy may have a beneficial effect of familiarizing the pregnant female to haemodynamic changes thus decreasing the risk of hypotension during various body positions.[10] Although, increased sympathetic function enhances the risk of hypertension and pre-eclampsia if there is dysregulation in the normal cardiovascular adaptations. About 12-20% of the maternal catecholamines cross the placenta and the remaining are metabolized. The placenta plays an imperative role in preventing maternal catecholamines from crossing the placenta to the foetal side.

Pregnancy and Adaptations of Placenta

The placenta plays a role of sensor to maintain the normal physiological needs of the foetus through physiological adaptations to maintain adequate foetal growth and development. The placenta control nutrient uptake, waste elimination and gas exchange between maternal and foetal interfaces. Human placental lactogen increases during the second trimester of the pregnancy and stimulates lipolysis, liberating maternal free fatty acids in order to provide an alternate source of energy for the mother to conserve glucose for foetal usage.[11] The enhanced free fatty acid may interfere with the insulin-directed entry of glucose into the maternal cells, thus human placental lactogen is a major antagonist of insulin action during pregnancy[11] and results in the development of gestational diabetes mellitus.

Pregnancy and Insulin Sensitivity and Resistance

In the 21st century, one of the most challenging issues for the physicians is to manage diabetes mellitus mainly Gestational Diabetes Mellitus (GDM). The occurrence of GDM varies substantially between populations however, as per IDF report, it affects approximately 15% of pregnant women worldwide.[12] Pregnancy causes reduced peripheral insulin sensitivity and enhances diabetogenic hormones including "oestrogen, progesterone, prolactin, human placental lactogen and cortisol" which are more marked in GDM to complete the metabolic requirements of the foetus and mother.[13] The cascade of consequent hormonal events promotes an upsurge in maternal blood glucose, reduced liver glycogen with an advancement in liver glucose and increased insulin production. In the second to third trimester, maternal fat deposition increases leading to insulin resistance and decreases 45-70% insulin sensitivity.[14] Insulin resistance may also be linked to fat mass accumulation which causes decrease utilization of maternal glucose to reserve additional glucose for foetal use. This reworking is a part of normal metabolic physiology as feto-placental part uses 30-50% of the maternal glucose pool in the third trimester for growth and development.[15] Inconsistency in the metabolic mechanisms causes gestational diabetes mellitus.

Pregnancy and Gestational Diabetes Mellitus

Many pregnant females normalize blood glucose levels

with adequate β-cell compensatory mechanism to produce additional insulin.[16] Pregnancy influenced insulin resistance is accompanied with metabolic dysregulation, carbohydrate intolerance, β-cell dysfunction and GDM. Females with Gestational Diabetes Mellitus are at greater risk for pregnancy and delivery complications including infant macrosomia, neonatal hypoglycaemia and caesarean delivery, postpartum haemorrhage, vaginal laceration[16] and type 2 DM.[17] β-cell dysfunction persists after the GDM pregnancy and excessive maternal weight gain are strong contributors to long-term metabolic dysfunction. Metabolic dysfunctions and obesity have been associated with an increased risk of type 2 DM after GDM pregnancy. Women who have had GDM have increased dyslipidaemia, high incidence of pregnancy-induced hypertension and risk for cardiovascular diseases.[18]

Conclusion

The metabolic physiology during pregnancy is the normal adaptations in which maternal body changes its physiological and homeostatic mechanisms to provide and ensure the basic foetal physiological needs for its survival and adequate growth. The metabolic changes, prepare the mother's body physiology for pregnancy, childbirth and lactation. However, if the maternal metabolic physiology during pregnancy is disturbed, it can cause increased fat accumulation, decreased insulin sensitivity, increased insulin resistance, gestational diabetes mellitus and also type 2 diabetes mellitus. It is suggested that, physicians should brief the pregnant females about healthy and physically active life style to prevent the diseases both in mother and foetus.

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